

Application No. 10/800350

Docket No.: VASG-P01-002

**AMENDMENTS TO THE CLAIMS:**

Please cancel withdrawn claims 35-37. This listing of claims will replace all prior versions and listings of claims in the application:

**Listing of Claims:**

1-25. (Canceled)

26. (Previously presented) An isolated monoclonal antibody which binds to an extracellular domain of an EphB4 protein and promotes apoptosis in a tumor cell, wherein the antibody is selected from bispecific, single-chain, chimeric, human, and humanized antibodies.

27. (Previously presented) The antibody of claim 26, wherein the antibody inhibits the interaction between Ephrin B2 and EphB4.

28. (Previously presented) The antibody of claim 26, wherein the antibody inhibits clustering of EphB4.

29. (Previously presented) The antibody of claim 26, wherein the antibody inhibits phosphorylation of EphB4.

30-31. (Canceled)

32. (Previously presented) A pharmaceutical composition comprising the antibody of claim 26, and a pharmaceutically acceptable carrier.

33. (Previously presented) A cosmetic composition comprising the antibody of claim 26, and a pharmaceutically acceptable carrier.

34. (Previously presented) A diagnostic kit comprising the antibody of claim 26, and a carrier.

35-37. (Canceled)

38. (Withdrawn) A method of reducing the growth rate of a tumor, comprising administering an amount of a polypeptide agent sufficient to reduce the growth rate of the tumor, wherein the polypeptide agent is selected from the group consisting of:

(a) a soluble polypeptide comprising an amino acid sequence of an extracellular domain of an EphB4 protein, wherein the EphB4 polypeptide is a monomer and binds specifically to an Ephrin B2 polypeptide;

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- (b) a soluble polypeptide comprising an amino acid sequence of an extracellular domain of an Ephrin B2 protein, wherein the soluble Ephrin B2 polypeptide is a monomer and binds with high affinity to an EphB4 polypeptide.
  - (c) an antibody which binds to an extracellular domain of an EphB4 protein and inhibits an activity of the EphB4; and
  - (d) an antibody which binds to an extracellular domain of an Ephrin B2 protein and inhibits an activity of the Ephrin B2.
39. (Withdrawn) The method of claim 38, wherein the tumor comprises cells expressing a higher level of EphB4 and/or EphrinB2 than noncancerous cells of a comparable tissue.
40. (Withdrawn) A method for treating a patient suffering from a cancer, comprising administering to the patient a polypeptide agent selected from the group consisting of:
- (a) a soluble polypeptide comprising an amino acid sequence of an extracellular domain of an EphB4 protein, wherein the EphB4 polypeptide is a monomer and binds specifically to an Ephrin B2 polypeptide;
  - (b) a soluble polypeptide comprising an amino acid sequence of an extracellular domain of an Ephrin B2 protein, wherein the soluble Ephrin B2 polypeptide is a monomer and binds with high affinity to an EphB4 polypeptide.
  - (c) an antibody which binds to an extracellular domain of an EphB4 protein and inhibits an activity of the EphB4; and
  - (d) an antibody which binds to an extracellular domain of an Ephrin B2 protein and inhibits an activity of the Ephrin B2.
41. (Withdrawn) The method of claim 40, wherein the cancer comprises cancer cells expressing EphrinB2 and/or EphB4 at a higher level than noncancerous cells of a comparable tissue.
42. (Withdrawn) The method of claim 40, wherein the cancer is metastatic cancer.
43. (Withdrawn) The method of claim 40, wherein the tumor is selected from the group consisting of colon carcinoma, breast tumor, mesothelioma, prostate tumor, squamous cell carcinoma, Kaposi sarcoma, and leukemia.

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44. (Withdrawn) The method of claim 40, wherein the cancer is an angiogenesis-dependent cancer.
45. (Withdrawn) The method of claim 40, wherein the cancer is an angiogenesis-independent cancer.
46. (Withdrawn) The method of claim 40, wherein the polypeptide agent inhibits the interaction between Ephrin B2 and EphB4.
47. (Withdrawn) The method of claim 40, wherein the polypeptide agent inhibits clustering of Ephrin B2 or EphB4.
48. (Withdrawn) The method of claim 40, wherein the polypeptide agent inhibits phosphorylation of Ephrin B2 or EphB4.
49. (Withdrawn) The method of claim 40, wherein the polypeptide agent is formulated with a pharmaceutically acceptable carrier.
50. (Withdrawn) The method of claim 40, further including administering at least one additional anti-cancer chemotherapeutic agent that inhibits cancer cells in an additive or synergistic manner with the polypeptide agent.
51. (Withdrawn) A method of inhibiting angiogenesis, comprising contacting a cell an amount of a polypeptide agent sufficient to inhibit angiogenesis, wherein the polypeptide agent is selected from the group consisting of:
  - (a) a soluble polypeptide comprising an amino acid sequence of an extracellular domain of an EphB4 protein, wherein the EphB4 polypeptide is a monomer and binds specifically to an Ephrin B2 polypeptide;
  - (b) a soluble polypeptide comprising an amino acid sequence of an extracellular domain of an Ephrin B2 protein, wherein the soluble Ephrin B2 polypeptide is a monomer and binds with high affinity to an EphB4 polypeptide.
  - (c) an antibody which binds to an extracellular domain of an EphB4 protein and inhibits an activity of the EphB4; and
  - (d) an antibody which binds to an extracellular domain of an Ephrin B2 protein and inhibits an activity of the Ephrin B2.

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52. (Withdrawn) The method of claim 51, wherein the cell expresses EphB4 or Ephrin B2.
53. (Withdrawn) A method for treating a patient suffering from an angiogenesis-associated disease, comprising administering to the patient a polypeptide agent selected from the group consisting of:
- (a) a soluble polypeptide comprising an amino acid sequence of an extracellular domain of an EphB4 protein, wherein the EphB4 polypeptide is a monomer and binds specifically to an Ephrin B2 polypeptide;
  - (b) a soluble polypeptide comprising an amino acid sequence of an extracellular domain of an Ephrin B2 protein, wherein the soluble Ephrin B2 polypeptide is a monomer and binds with high affinity to an EphB4 polypeptide.
  - (c) an antibody which binds to an extracellular domain of an EphB4 protein and inhibits an activity of the EphB4; and
  - (d) an antibody which binds to an extracellular domain of an Ephrin B2 protein and inhibits an activity of the Ephrin B2.
54. (Withdrawn) The method of claim 53, wherein the soluble polypeptide is formulated with a pharmaceutically acceptable carrier.
55. (Withdrawn) The method of claim 53, wherein the angiogenesis-associated disease is selected from the group consisting of angiogenesis-dependent cancer, benign tumors, inflammatory disorders, chronic articular rheumatism and psoriasis, ocular angiogenic diseases, Osler-Webber Syndrome, myocardial angiogenesis, plaque neovascularization, telangiectasia, hemophiliac joints, angiofibroma, wound granulation, wound healing, telangiectasia psoriasis scleroderma, pyogenic granuloma, coronary collaterals, ischemic limb angiogenesis, rubeosis, arthritis, diabetic neovascularization, fractures, vasculogenesis, and hematopoiesis.
56. (Withdrawn) The method of claim 53, further including administering at least one additional anti-angiogenesis agent that inhibits angiogenesis in an additive or synergistic manner with the soluble polypeptide.
- 57-62. (Canceled)
63. (Previously presented) An isolated cell expressing the antibody of claim 26.
64. (Previously presented) A non-human transgenic animal expressing the antibody of claim 26.

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- 65. (Previously presented) The antibody of claim 26, further comprising a label attached thereto.
- 66. (Previously presented) The antibody of claim 65, wherein the label is selected from a radioisotope, a fluorescent compound, an enzyme, or an enzyme co-factor.
- 67. (Previously presented) The antibody of claim 26, wherein the antibody inhibits angiogenesis.
- 68. (Previously presented) The antibody of claim 26, wherein the antibody promotes tumor regression.